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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/462,408	04/10/2000	GUNTER SCHMIDT	020600-283	5060

21839 7590 02/05/2004

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EXAMINER
FORMAN, BETTY J

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 02/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

PTO-90C (Rev. 10/03)

Office Action Summary	Application No. 09/462,408	Applicant(s) SCHMIDT ET AL.
	Examiner BJ Forman	Art Unit 1634

-- The MAILING DATE of this communication appears n the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 08 December 2003.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-18,20-24,27 and 28 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-18,20-24,27 and 28 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8 December 2003 has been entered.

Status of the Claims

2. This action is in response to papers filed 8 December 2003 in which claims 1, 21, 22, 23, 24, 27 and 28 were amended. All of the amendments have been thoroughly reviewed and entered.

The previous rejections in the Office Action dated 8 August 2003 are withdrawn in view of the amendments. All of the arguments have been thoroughly reviewed but are deemed moot in view of the amendments, withdrawn rejections and new grounds for rejection. New grounds for rejection are discussed.

Claims 1-18, 20-24 and 27-28 are under prosecution.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claim 1 is rejected under 35 U.S.C. 103(a) as obvious over Southern et al. (WO95/04160, published 9 February 1995) in view of Smith, L. M. (Nature, 1991, 349: 812-813) and Withers et al (U.S. Patent No. 5,716,812, issued 10 February 1998).

Regarding Claim 1, Southern et al. teach a method for characterizing DNA comprising: providing a population of DNA fragments, each having cleavably attached thereto a mass label for identifying a feature of that fragment; separating the fragments on the basis of their length i.e. separating by hybridizing the fragments to immobilized oligonucleotides of known length and at spaced locations on the support (page 20, lines 7-19); cleaving each fragment in a mass spectrometer to release its mass label; and determining each mass label by mass spectroscopy to identify the fragment (page 20, line 7-page 21, line 23) wherein the length of the fragment is "read" by repeating the above steps (page 21, lines 16-23) thereby "relating" the feature of each fragment to the length of the fragment to characterize the DNA. The preceding rejection is based on judicial precedent following In re Fitzgerald, 205 USPQ 594 because Southern et al. is silent with regard to relating the feature of each fragment to the length of the fragment. However, relating the feature to the length of the fragment recited in Claims 1-26 is deemed to be inherent in the detecting the mass labels (i.e. feature) in Southern et al. because the labels of Southern et al. identify each feature (i.e. labeled probe) of the fragment and number of features of the fragment wherein each feature has a known length (page 2, lines 26-33) and therefore, detecting the labels, detects the number of features of known length and hence identifies the length of the fragment.

Southern et al. teach the wherein the length of the fragment is "read" by repeating the above steps (page 21, lines 16-23) but they do not teach the method of separating the fragments is effected by capillary electrophoresis on the basis of their length.

However, length-based separation using capillary electrophoresis was well know in the art at the time the claimed invention was made as taught by Smith who teaches capillary electrophoresis provides for rapid and sensitive analysis of long DNA sequences (page 812, left column, second paragraph). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the separation of Southern et al. with the capillary electrophoresis taught by Smith for the expected benefits taught by the latter i.e. rapid analysis of long DNA sequences (page 812, left column, second paragraph).

Southern et al teach cleaving each fragment in a mass spectrometer to release its mass label; and determining each mass label by mass spectroscopy to identify the fragment (page 20, line 7-page 21, line 23) but they do not teach the cleavage is via collision. However, cleaving fragments in a mass spectrophotometer by collision was well known in the art at the time the claimed invention was made as taught by Withers et al. Withers et al further teach a motivation to use collision cleavage i.e. collision cleavage is sufficient to break the ester bond between the mass label and the fragment but does not break bonds within the fragment (Column 19, lines 38-45). Therefore, It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the collision cleavage taught by Withers et al to the mass label cleavage of Southern et al for the expected benefit of mass label-cleavage without damaging the fragment as taught by Withers et al (Column 19, lines 38-45).

5. Claims 2-18 and 20-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Southern et al. (WO95/04160, published 9 February 1995) in view of Ness et al. (U.S. Patent No. 6,027,890, filed 22 July 1997), Alberts (Molecular Biology of the Cell, 1994, page 298); Smith, L. M. (Nature, 1991, 349: 812-813) and Withers et al (U.S. Patent No. 5,716,812, issued 10 February 1998). As stated above, the claims are replete with relative, non-specific, redundant and undefined terms and phrases. For purposes of examination, the examiner has interpreted the claims as noted below.

Regarding Claim 2, Southern et al. teach the method further comprises providing at least one DNA single-stranded temple with a primer and generating the population of DNA fragments from the template wherein the population comprises at least one series of fragments wherein the feature of each fragment determined by each mass label relates to a nucleotide at one end of each fragment so that each nucleotide is related to a position in the template associated with the label so as to deduce the sequence of the template (Fig. 5) but they do not teach the series of fragments contains all possible lengths of a second strand of DNA complementary to the template. However, Ness et al. teach a similar method comprising: providing a population of DNA fragments, separating the fragments based on their length, cleaving each fragment; and determining the mass label to identify the fragment (Column 2, lines 55-67) wherein the fragments contains all possible length of a second strand DNA complementary to the template i.e. primer extension and incorporation of dideoxynucleotides (Column 53, lines 34-57) and it was known in the art at the time the claimed invention was made that primer extension dideoxynucleotide incorporation provided a series of fragments that contains all possible lengths of the template as taught by Alberts et al. (page 298). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the population of DNA fragments of Southern et al. and to provide fragments having all possible lengths as taught by Ness et al. for the obvious benefit of

characterizing DNA of interest completely by characterizing complementary fragments of all possible lengths.

Southern et al. teach the method wherein the length of the fragment is "read" by repeating the above steps (page 21, lines 16-23) but they do not teach the method of separating the fragments is effected by capillary electrophoresis. However, capillary electrophoresis was well know in the art at the time the claimed invention was made as taught by Smith who teaches capillary electrophoresis provides for rapid analysis of long DNA sequences (page 812, left column, second paragraph). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the separation of Southern et al. with the capillary electrophoresis taught by Smith for the expected benefits taught by the latter i.e. rapid analysis of long DNA sequences (page 812, left column, second paragraph).

Southern et al teach cleaving each fragment in a mass spectrometer to release its mass label; and determining each mass label by mass spectroscopy to identify the fragment (page 20, line 7-page 21, line 23) but they do not teach the cleavage is via collision. However, cleaving fragments in a mass spectrophotometer by collision was well known in the art at the time the claimed invention was made as taught by Withers et al. Withers et al further teach a motivation to use collision cleavage i.e. collision cleavage is sufficient to break the ester bond between the mass label and the fragment but does not break bonds within the fragment (Column 19, lines 38-45). Therefore, It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the collision cleavage taught by Withers et al to the mass label cleavage of Southern et al for the expected benefit of mass label-cleavage without damaging the fragment as taught by Withers et al (Column 19, lines 38-45).

Regarding Claim 3, Southern et al. teach the method wherein the series of DNA fragments is provided by contacting the template in the presence of DNA enzyme with a mixture of nucleotides sufficient for hybridizing to the template for forming a second strand of

DNA complementary to the template and wherein the mixture further comprises a set of probes containing all four nucleotides wherein the probes comprise modified nucleotides and wherein the probes have a mass label cleavably attached and are blocked to prevent further polymerization (page 3, lines 24-32 and page 20, line 32-page 21, line 3) but they do not teach the DNA enzyme is a DNA polymerase. However, Ness et al. teach the similar method wherein the series of DNA fragments are provided by contacting the in the presence of ligating or polymerizing enzymes (i.e. DNA polymerase, Column 3, lines 21-29). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the DNA enzyme of Southern et al. with the DNA polymerase of Ness et al. for the expected benefit of incorporating dideoxynucleotides to provide fragments having all possible lengths thereby to characterizing DNA of interest completely by characterizing complementary fragments of all possible lengths.

Regarding Claim 4, Southern et al. teach the method wherein the template is a plurality of template and the DNA fragments is provided by contacting each template in a separate reaction vessel (i.e. spaced location) in the presence of a DNA enzyme with a mixture of nucleotides sufficient for hybridizing to the template to form a second strand of DNA complementary to the template and wherein the mixture further comprises a set of four probes containing all four nucleotides wherein the nucleotide of each probe comprises modified nucleotide which hybridizes to the second strand of DNA but is blocked to prevent further polymerization and has a mass label cleavably attached (page 3, lines 24-32, page 7, lines 26-34 and page 20, line 32-page 21, line 3) wherein the mass labels differ from other sets of labels (page 2, lie 33-page 3, line 9) and wherein the fragments are pooled before step (ii) i.e. before immobilization on (page 20, lines 11-16) but they do not teach the DNA enzyme is a DNA polymerase. However, Ness et al. teach the similar method wherein the DNA enzyme is a DNA polymerase (Column 3, lines 21-29).

Regarding Claim 5, Southern et al. teach the method wherein the template is a plurality of template and the DNA fragments are provided by contacting each template in a separate reaction vessel (i.e. spaced location) in the presence of a DNA enzyme with a mixture of nucleotides sufficient for hybridizing to the template to form a second strand of DNA complementary to the template wherein the mixture further comprises probes comprising modified nucleotides which hybridizes to the second strand of DNA but is blocked to prevent further polymerization and has a mass label cleavably attached (page 3, lines 24-32, page 7, lines 26-34 and page 20, line 32-page 21, line 3) wherein the mass labels differ from other sets of labels (page 2, lie 33-page 3, line 9) and wherein the fragments are pooled before step (ii) i.e. before immobilization on (page 20, lines 11-16) wherein the probe contains only one of the four nucleotides (Example 16b, page 44, lines 12-16) but they do not teach the DNA enzyme is a DNA polymerase. However, Ness et al. teach the similar method wherein the DNA enzyme is a DNA polymerase (Column 3, lines 21-29).

Regarding Claim 6, Southern et al. teach the method wherein the template is a plurality of templates and the DNA fragments are provided by contacting the templates in a separate reaction vessels (i.e. spaced location) in the presence of a DNA enzyme with a mixture of nucleotides sufficient for hybridizing to the template for forming a second strand of DNA complementary to the template and wherein the mixture further comprises probes comprising modified nucleotides wherein the nucleotide of each probe comprises modified nucleotide which hybridizes to the second strand of DNA but is blocked to prevent further polymerization and has a mass label cleavably attached (page 3, lines 24-32, page 7, lines 26-34 and page 20, line 32-page 21, line 3) wherein the mass labels differ from other sets of labels (page 2, lie 33-page 3, line 9) wherein the probe contains only one of the four nucleotides (Example 16b, page 44, lines 12-16) but do not teach the DNA enzyme is a DNA polymerase. However, Ness et al. teach the similar method wherein the DNA enzyme is a DNA polymerase (Column 3, lines 21-29).

Regarding Claim 7, Southern et al. teach the method wherein the template is four sets of single-stranded DNA templates (page 5, lines 27-35) wherein the DNA fragments are provided by contacting each template in a separate reaction vessel (i.e. spaced location) in the presence of a DNA enzyme with a mixture of nucleotides sufficient for hybridizing to the template for forming a second strand of DNA complementary to the template and wherein the mixture further comprises probes comprising modified nucleotides which hybridize to the second strand of DNA but are blocked to prevent further polymerization, wherein each fragment is terminated with the probe and wherein each of the templates is primed with a primer (i.e. linker) to which the mass label is cleavably attached (by ligation of the probe comprising the mass label to the linker) (page 3, lines 24-32, page 7, lines 26-34 and page 20, line 32-page 21, line 3) wherein the mass labels differ from other sets of labels (page 2, lie 33-page 3, line 9) and wherein the fragments are pooled before step (ii) i.e. before immobilization on (page 20, lines 11-16) wherein the probe contains only one of the four nucleotides i.e. wherein the probe is chosen to identify a specific position of the analyte chain (page 2, lines 2-8 and 26-32) but they do not teach the DNA enzyme is a DNA polymerase. However, Ness et al. teach the similar method wherein the DNA enzyme is a DNA polymerase (Column 3, lines 21-29).

Regarding Claim 8, Southern et al. teach the method wherein the template is a plurality of template and the DNA fragments is provided by contacting each template in a separate reaction vessel (i.e. spaced location) in the presence of a DNA enzyme with a mixture of nucleotides sufficient for hybridizing to the template for forming a second strand of DNA complementary to the template and wherein the mixture further comprises a set of four probes containing all four nucleotides wherein the nucleotide of each probe comprises modified nucleotide which hybridizes to the second strand of DNA but is blocked to prevent further polymerization and has a mass label cleavably attached (page 3, lines 24-32, page 7, lines 26-34 and page 20, line 32-page 21, line 3) wherein the mass labels are uniquely resolvable in a

mass spectrometer (page 2, line 33-page 3, line 9) and wherein the fragments are pooled before step (ii) (i.e. before immobilization, page 20, lines 11-16) and sorted according to sub-sequence (i.e. according to vector sequence, page 17, lines 8-11) wherein the fragments are immobilized in sets (i.e. groups) to facilitate detection and simplify identification (page 18, lines 10-17) and wherein the fragments have a common sub-sequence length of 3-5 bases (i.e. the reporter groups adjacent to the linker (i.e. primer) comprise 2-20 residues, page 2, lines 26-33) but they do not teach the DNA enzyme is a DNA polymerase. However, Ness et al. teach the similar method wherein the DNA enzyme is a DNA polymerase (Column 3, lines 21-29).

Regarding Claim 9, Southern et al. teach the method wherein the series of DNA fragment is provided by contacting the template in the presence of a DNA enzyme with a mixture of nucleotides sufficient for hybridizing to the template to form a second strand of DNA complementary to the template, wherein the mixture further comprises a set of four probes containing all four nucleotides for hybridizing to the templates in which a nucleotide of each probe comprises a modified nucleotide which is capable of polymerizing (hybridizing) to the second strand of DNA but reversibly blocked (i.e. removable) to prevent further polymerization wherein the step of contacting forms a series of templates, each second strand terminated with one of the probes; removing unincorporated nucleotide; unblocking the modified nucleotides; and contacting the templates with an array of probes wherein each probe has a nucleotide sequence of common length of 2 to 6 (page 2, lines 27-33 and Fig. 5) wherein each probe is cleavably attached to a mass label which is uniquely resolvable in mass spectrometry for identifying the nucleotide sequence (page 20, lines 7-36) but they do not teach the DNA enzyme is a DNA polymerase and they do not teach that contacting the template forms all possible lengths of second strand DNA. However, Ness et al. teach the similar method wherein the DNA enzyme is a DNA polymerase (Column 3, lines 21-29) and wherein the fragments contains all possible length of a second strand DNA complementary to the template i.e. primer extension and incorporation of dideoxynucleotides (Column 53, lines 34-57) and it was known in the art

at the time the claimed invention was made that primer extension dideoxynucleotide incorporation provided a series of fragments that contains all possible lengths of the template as taught by Alberts et al. (page 298).

Regarding Claim 10, Southern et al. teach the method wherein the template is a plurality of primer DNA single-stranded templates, each at a unique concentration (i.e. the templates are immobilized either singly or in small sets i.e. at a known or unique concentration) wherein the series of DNA fragment is provided by contacting the templates in the presence of a DNA enzyme with a mixture of nucleotides sufficient for hybridizing to the template to form a second strand of DNA complementary to the templates, wherein the mixture further comprises a set of four probes containing all four nucleotides for hybridizing to the templates in which a nucleotide of each probe comprises a modified nucleotide which is capable of (hybridizing) to the second strand of DNA but reversibly blocked (i.e. removable) to prevent further polymerization wherein the step of contacting forms a series of templates, each second strand terminated with one of the probes; removing unincorporated nucleotide; unblocking the modified nucleotides; and contacting the templates with an array of probes wherein each probe has a nucleotide sequence of common length of 2 to 6 (page 2, lines 27-33) wherein each probe is cleavably attached to a mass label which is uniquely resolvable in mass spectrometry for identifying the nucleotide sequence (page 20, lines 7-36) but they do not teach the DNA enzyme is a DNA polymerase and they do not teach that contacting the template forms all possible lengths of second strand DNA. However, Ness et al. teach the similar method wherein the DNA enzyme is a DNA polymerase (Column 3, lines 21-29) and wherein the fragments contains all possible length of a second strand DNA complementary to the template i.e. primer extension and incorporation of dideoxynucleotides (Column 53, lines 34-57) and it was known in the art at the time the claimed invention was made that primer extension dideoxynucleotide incorporation provided a series of fragments that contains all possible lengths of the template as taught by Alberts et al. (page 298).

Regarding Claim 11, Southern et al. teach the method wherein the series of DNA fragments is provided by contacting the template in the presence of DNA ligase with a mixture of oligonucleotides sufficient for hybridizing to the template for forming a second strand of DNA complementary to the template, the oligonucleotides each having a common length in the range of 2 to 6 (page 2, lines 27-33) wherein the mixture further comprise a set of probes containing all possible oligonucleotides of common length for hybridizing to the templates in which the oligonucleotide of each probe comprises a modified oligonucleotide which is capable of ligating to the second strand of DNA but blocked to prevent further ligation thereto and which is cleavably attached to a uniquely resolvable mass label for identifying the oligonucleotide and wherein each fragment is terminated with one of the probes (page 3, line 32-page 4, line 6, page 20, lines 7-36 and Fig 5) but they do not teach the series of DNA fragments comprises all possible lengths of second strand DNA and they do not teach oligonucleotides of a common length 1. However, Ness et al. teach the similar method wherein the oligonucleotide of the common length 1 (i.e. dideoxynucleotides) and wherein the fragments contains all possible length of a second strand DNA complementary to the template i.e. primer extension and incorporation of dideoxynucleotides (Column 53, lines 34-57) and it was known in the art at the time the claimed invention was made that primer extension dideoxynucleotide incorporation provided a series of fragments that contains all possible lengths of the template as taught by Alberts et al. (page 298).

Regarding Claim 12, Southern et al. teach the method wherein the template is a plurality of primer DNA single-stranded templates, each at a unique concentration (i.e. the templates are immobilized either singly or in small sets i.e. at a known or unique concentration) wherein the series of DNA fragment is provided by contacting the template in the presence of a DNA ligase with a mixture of oligonucleotides sufficient for hybridizing to the templates to form a second strand of DNA complementary to the templates, the oligonucleotides each having a common length of 2 to 6 (page 2, lines 27-33) wherein the

mixture further comprises a set of probe containing all possible oligonucleotides of the common length wherein the oligonucleotide of each probe comprises a modified oligonucleotide which is capable of ligating to the second strand of DNA but blocked to prevent further ligation thereto and which is cleavably attached to a uniquely resolvable mass label for identifying the modified oligonucleotide and wherein each fragment is terminated with one of the probes (page 3, line 32-page 4, line 6, page 20, lines 7-36 and Fig 5) but they do not teach the series of DNA fragments comprises all possible lengths of second strand DNA and they do not teach oligonucleotides of a common length 1. However, Ness et al. teach the similar method wherein the oligonucleotide of the common length 1 (i.e. dideoxynucleotides) and wherein the fragments contains all possible length of a second strand DNA complementary to the template i.e. primer extension and incorporation of dideoxynucleotides (Column 53, lines 34-57) and it was known in the art at the time the claimed invention was made that primer extension dideoxynucleotide incorporation provided a series of fragments that contains all possible lengths of the template as taught by Alberts et al. (page 298).

Regarding Claim 13, Southern et al. teach the method wherein the plurality of single-stranded templates is primed by hybridizing to a known sub-sequence common to each of the templates and array of primers each comprising a base sequence containing a common sequence complementary to the known sub-sequence (i.e. primer (linker) is a vector sequence which is common to all the clones, page 15, lines 23-28) and a variable sequence of common length in the range of 2 to 6 (page 2, lines 27-33 and Fig. 5) in which the array contains all possible sequences of that common length and the mass label cleavable attached to each primer is relatable to the variable sequences which is relatable to the template to be sequenced (page 16, lines 6-10).

Regarding Claim 14, Southern et al. teach the method wherein the step of sorting the pooled fragments comprises contacting the fragments with an array of spatially separate oligonucleotides each comprising a base sequence containing a common sequence

complementary to the primer sequence and a variable sequence (i.e. a vector sequence plus the clone, page 15, lines 23-28) of the common length which array contains all possible variable sequences of the common length (page 15, lines 20-36).

Regarding Claim 15, Southern et al. teach the reaction vessels are spaced locations on a support (page 20, lines 11-12) but they do not teach the locations are separate containers. Ness et al. teach the similar method wherein the reaction is PCR (Column 3, lines 21-28), but they are silent with regard to the reaction vessel of the PCR reaction. However, PCR reactions separate containers wherein the container are the "reaction vessel" was known and routinely practiced in the art at the time the claimed invention was made. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the reaction vessel of Southern et al. with the routinely practiced PCR separate container reaction vessel in the PCR reaction of Ness et al. for the obvious benefit of isolating the reactions to prevent cross-contamination between the reactions.

Regarding Claim 16, Southern et al. teach the method wherein the mixture of nucleotides comprises ATP, GTP, TTP, and CTP (Fig. 5).

Regarding Claim 17, Southern et al. teach the modified nucleotides are deoxynucleotides (DNA) (Fig. 5).

Regarding Claim 18, Southern et al. teach the method wherein the primed DNA is immobilized on a solid support (page 20, lines 11-20).

Regarding Claim 20, Southern et al. teach the method wherein each mass label is cleavably attached to a fragment by a linker cleavable in a mass spectrometer (page 9, lines 29-34).

Regarding Claim 21, Southern et al. teach a method for characterizing DNA comprising: providing a primed DNA single-stranded template; contacting the template in the presence of a DNA enzyme with a mixture of nucleotides sufficient for hybridizing to the template for forming a second strand of DNA complementary to the template, wherein the mixture further comprises

a set of four probes containing all four nucleotides for hybridizing to the templates in which a nucleotide of each probe comprises a modified nucleotide which is capable of polymerizing (hybridizing) to the second strand of DNA but reversibly blocked to prevent further polymerization thereto, wherein the step of contacting forms a series of templates, each terminated with one of the probes; removing unincorporated nucleotides; unblocking the modified nucleotides; contacting the templates with an array of oligonucleotide probes to form a series of fragments, each probe having a sequence of common length of 2 to 6 (page 2, lin2 27-33) wherein each probe is cleavably attached to a uniquely resolvable mass label for identifying the nucleotide sequence; separating the fragments from one another; cleaving each fragment to release the mass label; and determining each mass label by mass spectrometry to relate its sequence to a position in the template so as to deduce the sequence of the template (page 15, line 20-page 16, line 25) but they do not teach the DNA enzyme is a DNA polymerase. However, Ness et al. teach the similar method wherein the series of DNA fragments are provided by contacting the in the presence of ligating or polymerizing enzymes (i.e. DNA polymerase, Column 3, lines 21-29). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the DNA enzyme of Southern et al. with the DNA polymerase of Ness et al. for the expected benefit of incorporating dideoxynucleotides to provide fragments having all possible lengths thereby to characterizing DNA of interest completely by characterizing complementary fragments of all possible lengths.

Southern et al. teach the method wherein the length of the fragment is "read" by repeating the above steps (page 21, lines 16-23) but they do not teach the method of separating the fragments is effected by capillary electrophoresis. However, capillary electrophoresis was well know in the art at the time the claimed invention was made as taught by Smith who teaches capillary electrophoresis provides for rapid analysis of long DNA sequences (page 812, left column, second paragraph). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the separation of Southern et al. with the

capillary electrophoresis taught by Smith for the expected benefits taught by the latter i.e. rapid analysis of long DNA sequences (page 812, left column, second paragraph).

Southern et al teach cleaving each fragment in a mass spectrometer to release its mass label; and determining each mass label by mass spectroscopy to identify the fragment (page 20, line 7-page 21, line 23) but they do not teach the cleavage is via collision. However, cleaving fragments in a mass spectrophotometer by collision was well known in the art at the time the claimed invention was made as taught by Withers et al. Withers et al further teach a motivation to use collision cleavage i.e. collision cleavage is sufficient to break the ester bond between the mass label and the fragment but does not break bonds within the fragment (Column 19, lines 38-45). Therefore, It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the collision cleavage taught by Withers et al to the mass label cleavage of Southern et al for the expected benefit of mass label-cleavage without damaging the fragment as taught by Withers et al (Column 19, lines 38-45).

Regarding Claim 22, Southern et al. teach a method for characterizing DNA comprising: providing a plurality of primed DNA single-stranded templates, each at a unique concentration (i.e. the templates are immobilized either singly or in small sets i.e. at a known or unique concentration); contacting the template in the presence of a DNA enzyme with a mixture of nucleotides sufficient for hybridizing to the template for forming a second strand of DNA complementary to the template, wherein the mixture further comprises a set of four probes containing all four nucleotides for hybridizing to the templates in which a nucleotide of each probe comprises a modified nucleotide which is capable of polymerizing (hybridizing) to the second strand of DNA but reversibly blocked to prevent further polymerization thereto, wherein the step of contacting forms a series of templates, each terminated with one of the probes; removing unincorporated nucleotides; unblocking the modified nucleotides; contacting the templates with an array of oligonucleotide probes to form a series of fragments, each probe

having a sequence of common length 2 to 6 (page 2, lines 27-33) wherein each probe is cleavably attached to a uniquely resolvable mass label for identifying the nucleotide sequence; separating the fragments from one another; cleaving each fragment to release the mass label; and determining each mass label by mass spectrometry to relate its sequence to a position in the template so as to deduce the sequence of the template (page 15, line 20-page 16, line 25) but they do not teach the DNA enzyme is a DNA polymerase. However, Ness et al. teach the similar method wherein the series of DNA fragments are provided by contacting the in the presence of ligating or polymerizing enzymes (i.e. DNA polymerase, Column 3, lines 21-29). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the DNA enzyme of Southern et al. with the DNA polymerase of Ness et al. for the expected benefit of incorporating dideoxynucleotides to provide fragments having all possible lengths thereby to characterizing DNA of interest completely by characterizing complementary fragments of all possible lengths.

Southern et al. teach the method wherein the length of the fragment is "read" by repeating the above steps (page 21, lines 16-23) but they do not teach the method of separating the fragments is effected by capillary electrophoresis. However, capillary electrophoresis was well know in the art at the time the claimed invention was made as taught by Smith who teaches capillary electrophoresis provides for rapid analysis of long DNA sequences (page 812, left column, second paragraph). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the separation of Southern et al. with the capillary electrophoresis taught by Smith for the expected benefits taught by the latter i.e. rapid analysis of long DNA sequences (page 812, left column, second paragraph).

Southern et al teach cleaving each fragment in a mass spectrometer to release its mass label; and determining each mass label by mass spectroscopy to identify the fragment (page 20, line 7-page 21, line 23) but they do not teach the cleavage is via collision. However, cleaving fragments in a mass spectrophotometer by collision was well known in the art at the time the

claimed invention was made as taught by Withers et al. Withers et al further teach a motivation to use collision cleavage i.e. collision cleavage is sufficient to break the ester bond between the mass label and the fragment but does not break bonds within the fragment (Column 19, lines 38-45). Therefore, It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the collision cleavage taught by Withers et al to the mass label cleavage of Southern et al for the expected benefit of mass label-cleavage without damaging the fragment as taught by Withers et al (Column 19, lines 38-45).

Regarding Claim 23, Southern et al. teach a method for characterizing DNA comprising: providing a primed DNA single-stranded template; contacting the template in the presence of DNA ligase with a mixture of oligonucleotides sufficient for hybridizing to the template for forming a second strand of DNA complementary to the template, the oligonucleotides each having a common length in the range 2 to 6 (page 2, lines 27-33 and Fig. 5), wherein the mixture further comprise a set of probes containing all possible oligonucleotides of common length for hybridizing to the templates in which the oligonucleotide of each probe comprises a modified oligonucleotide which is capable of ligating to the second strand of DNA but blocked to prevent further ligation thereto and which is cleavably attached to a uniquely resolvable mass label for identifying the oligonucleotide and wherein each fragment is terminated with one of the probes; separating the fragments by immobilization; cleaving each fragment to release its mass label; and determining each mass label by mass spectrometry to relate it corresponding oligonucleotide to a position in the template so as to deduce the sequence of the template. (page 15, line 20-page 16, line 25) but they do not teach the series of DNA fragments comprises all possible lengths of second strand DNA and they do not teach oligonucleotides of a common length 1. However, Ness et al. teach the similar method wherein the oligonucleotide of the common length 1 (i.e. dideoxynucleotides) and wherein the fragments contains all possible length of a second strand DNA complementary to the template i.e. primer extension and

incorporation of dideoxynucleotides (Column 53, lines 34-57) and it was known in the art at the time the claimed invention was made that primer extension dideoxynucleotide incorporation provided a series of fragments that contains all possible lengths of the template as taught by Alberts et al. (page 298).

Southern et al. teach the method wherein the length of the fragment is "read" by repeating the above steps (page 21, lines 16-23) but they do not teach the method of separating the fragments is effected by capillary electrophoresis. However, capillary electrophoresis was well know in the art at the time the claimed invention was made as taught by Smith who teaches capillary electrophoresis provides for rapid analysis of long DNA sequences (page 812, left column, second paragraph). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the separation of Southern et al. with the capillary electrophoresis taught by Smith for the expected benefits taught by the latter i.e. rapid analysis of long DNA sequences (page 812, left column, second paragraph).

Southern et al teach cleaving each fragment in a mass spectrometer to release its mass label; and determining each mass label by mass spectroscopy to identify the fragment (page 20, line 7-page 21, line 23) but they do not teach the cleavage is via collision. However, cleaving fragments in a mass spectrophotometer by collision was well known in the art at the time the claimed invention was made as taught by Withers et al. Withers et al further teach a motivation to use collision cleavage i.e. collision cleavage is sufficient to break the ester bond between the mass label and the fragment but does not break bonds within the fragment (Column 19, lines 38-45). Therefore, It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the collision cleavage taught by Withers et al to the mass label cleavage of Southern et al for the expected benefit of mass label-cleavage without damaging the fragment as taught by Withers et al (Column 19, lines 38-45).

Regarding Claim 24, Southern et al. teach a method for characterizing DNA comprising: providing a primed DNA single-stranded template each at a unique concentration (i.e. the templates are immobilized either singly or in small sets i.e. at a known or unique concentration); contacting the template in the presence of DNA ligase with a mixture of oligonucleotides sufficient for hybridizing to the template for forming a second strand of DNA complementary to the template, the oligonucleotides each having a common length in the range 2 to 6 (page 2, lines 27-33 and Fig. 5), wherein the mixture further comprise a set of probes containing all possible oligonucleotides of common length for hybridizing to the templates in which the oligonucleotide of each probe comprises a modified oligonucleotide which is capable of ligating to the second strand of DNA but blocked to prevent further ligation thereto and which is cleavably attached to a uniquely resolvable mass label for identifying the oligonucleotide and wherein each fragment is terminated with one of the probes; separating the fragments by immobilization; cleaving each fragment to release its mass label; and determining each mass label by mass spectrometry to relate it corresponding oligonucleotide to a position in the template so as to deduce the sequence of the template. (page 15, line 20-page 16, line 25) but they do not teach the series of DNA fragments comprises all possible lengths of second strand DNA and they do not teach oligonucleotides of a common length 1. However, Ness et al. teach the similar method wherein the oligonucleotide of the common length 1 (i.e. dideoxynucleotides) and wherein the fragments contains all possible length of a second strand DNA complementary to the template i.e. primer extension and incorporation of dideoxynucleotides (Column 53, lines 34-57) and it was known in the art at the time the claimed invention was made that primer extension dideoxynucleotide incorporation provided a series of fragments that contains all possible lengths of the template as taught by Alberts et al. (page 298).

Southern et al. teach the method wherein the length of the fragment is "read" by repeating the above steps (page 21, lines 16-23) but they do not teach the method of separating

the fragments is effected by capillary electrophoresis. However, capillary electrophoresis was well know in the art at the time the claimed invention was made as taught by Smith who teaches capillary electrophoresis provides for rapid analysis of long DNA sequences (page 812, left column, second paragraph). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the separation of Southern et al. with the capillary electrophoresis taught by Smith for the expected benefits taught by the latter i.e. rapid analysis of long DNA sequences (page 812, left column, second paragraph).

Southern et al teach cleaving each fragment in a mass spectrometer to release its mass label; and determining each mass label by mass spectroscopy to identify the fragment (page 20, line 7-page 21, line 23) but they do not teach the cleavage is via collision. However, cleaving fragments in a mass spectrophotometer by collision was well known in the art at the time the claimed invention was made as taught by Withers et al. Withers et al further teach a motivation to use collision cleavage i.e. collision cleavage is sufficient to break the ester bond between the mass label and the fragment but does not break bonds within the fragment (Column 19, lines 38-45). Therefore, It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the collision cleavage taught by Withers et al to the mass label cleavage of Southern et al for the expected benefit of mass label-cleavage without damaging the fragment as taught by Withers et al (Column 19, lines 38-45).

6. Claim 27 is rejected under 35 U.S.C. 103(a) as being unpatentable over Southern et al. (WO95/04160, published 9 February 1995) in view of Ness et al. (U.S. Patent No. 6,027,890,

filed 22 July 1997), Smith, L. M. (Nature, 1991, 349: 812-813) and Withers et al (U.S. Patent No. 5,716,812, issued 10 February 1998).

Regarding Claim, 27 Southern et al. teach a method for characterizing DNA comprising: providing at least one DNA template primed with a primer; generating a population of fragments of said DNA from the template by contacting with a mixture of nucleotides to form a second strand of DNA complementary to the template wherein the mixture comprises a set of four probes containing all four nucleotides and wherein each probe comprises a modified nucleotide which blocks further polymerization and wherein the modified nucleotide is cleavably attached to a mass label for identifying the modified nucleotide (i.e. a nucleotide sequence to which a linker and tag are attached Fig. 3); separating the fragments on the basis of their length i.e. separating by hybridizing the fragments to immobilized oligonucleotides of known length and at spaced locations on the support (page 20, lines 7-19); cleaving each fragment in a mass spectrometer to release its mass label; and determining each mass label by mass spectroscopy to identify the fragment (page 20, line 7-page 21, line 23) wherein the length of the fragment is "read" by repeating the above steps (page 21, lines 16-23) thereby "relating" the feature of each fragment to the length of the fragment to characterize the DNA. The preceding rejection is based on judicial precedent following In re Fitzgerald, 205 USPQ 594 because Southern et al. is silent with regard to relating the feature of each fragment to the length of the fragment. However, relating the feature to the length of the fragment recited in Claims 1-26 is deemed to be inherent in the detecting the mass labels (i.e. feature) in Southern et al. because the labels of Southern et al. identify each feature (i.e. labeled probe) of the fragment and number of features of the fragment wherein each feature has a known length (page 2, lines 26-33) and therefore, detecting the labels, detects the number of features of known length and hence identifies the length of the fragment. The burden is on applicant to show that the claimed relating the feature to the length of the fragment is either different or non-obvious over that of Southern et al. Alternatively, it would have been obvious to one of

ordinary skill in the art at the time the claimed invention was made to apply the detection of mass labels in the method of Southern et al. wherein unique labels are attached to features (i.e. probes) of known length and wherein multiple labeled features (i.e. probes) are ligated to form a fragment to thereby detect the labels and number of labels to relate the labeled features to the length of the fragment. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made that the teaching of Southern et al. encompasses the claimed separating based on length because the sequence of the immobilized oligonucleotide is known, the length of the oligonucleotide is also known. While hybridization does not require perfect complementation in sequence and length, fragments that hybridize to the immobilized oligonucleotides of Southern et al. would, to at least some degree, complement the immobilized oligonucleotide in sequence and length. Therefore, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made that the fragments hybridized to the immobilized oligonucleotides at spaced locations on the support are spatially separated from other fragments based on their length. Southern et al. do not teach the series of fragments contains all possible lengths of a second strand of DNA complementary to the template. However, Ness et al. teach a similar method comprising: providing a population of DNA fragments, separating the fragments based on their length, cleaving each fragment; and determining the mass label to identify the fragment (Column 2, lines 55-67) wherein the fragments contains all possible length of a second strand DNA complementary to the template i.e. primer extension and incorporation of dideoxynucleotides (Column 53, lines 34-57) and it was known in the art at the time the claimed invention was made that primer extension dideoxynucleotide incorporation provided a series of fragments that contains all possible lengths of the template as taught by Alberts et al. (page 298). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the population of DNA fragments of Southern et al. and to provide fragments having all possible

lengths as taught by Ness et al. for the obvious benefit of characterizing DNA of interest completely by characterizing complementary fragments of all possible lengths.

Southern et al. teach the method wherein the length of the fragment is "read" by repeating the above steps (page 21, lines 16-23) but they do not teach the method of separating the fragments is effected by capillary electrophoresis. However, capillary electrophoresis was well know in the art at the time the claimed invention was made as taught by Smith who teaches capillary electrophoresis provides for rapid analysis of long DNA sequences (page 812, left column, second paragraph). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the separation of Southern et al. with the capillary electrophoresis taught by Smith for the expected benefits taught by the latter i.e. rapid analysis of long DNA sequences (page 812, left column, second paragraph).

Southern et al teach cleaving each fragment in a mass spectrometer to release its mass label; and determining each mass label by mass spectroscopy to identify the fragment (page 20, line 7-page 21, line 23) but they do not teach the cleavage is via collision. However, cleaving fragments in a mass spectrophotometer by collision was well known in the art at the time the claimed invention was made as taught by Withers et al. Withers et al further teach a motivation to use collision cleavage i.e. collision cleavage is sufficient to break the ester bond between the mass label and the fragment but does not break bonds within the fragment (Column 19, lines 38-45). Therefore, It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the collision cleavage taught by Withers et al to the mass label cleavage of Southern et al for the expected benefit of mass label-cleavage without damaging the fragment as taught by Withers et al (Column 19, lines 38-45).

7. Claim 28 is rejected under 35 U.S.C. 103(a) as being unpatentable over Southern et al. (WO95/04160, published 9 February 1995) in view of Ness et al. (U.S. Patent No. 6,027,890, filed 22 July 1997) and Withers et al (U.S. Patent No. 5,716,812, issued 10 February 1998).

Regarding Claim 28, Southern et al. teach a method for characterizing DNA comprising: providing at least one strand of the DNA as a single-stranded template primed with a set of oligonucleotide primers each primer comprising a mass label cleavably attached wherein each mass label is cleavable from the primer in a mass spectrometer and is uniquely resolvable in relation to every other mass label and generating a population of fragments from each template by contacting the template with a mixture of nucleotides complementary to the template wherein the feature of each fragment relates to a nucleotide sequence at the end of the fragment so as to deduce the sequence of the template and characterize the DNA (page 19, lines 4-24 and Claim 17). Southern et al. do not teach the series of fragments contains all possible lengths of a second strand of DNA complementary to the template. However, Ness et al. teach a similar method comprising: providing a population of DNA fragments, separating the fragments based on their length, cleaving each fragment; and determining the mass label to identify the fragment (Column 2, lines 55-67) wherein the fragments contains all possible length of a second strand DNA complementary to the template i.e. primer extension and incorporation of dideoxynucleotides (Column 53, lines 34-57) and it was known in the art at the time the claimed invention was made that primer extension dideoxynucleotide incorporation provided a series of fragments that contains all possible lengths of the template as taught by Alberts et al. (page 298). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the population of DNA fragments of Southern et al. and to provide fragments having all possible lengths as taught by Ness et al. for the obvious benefit of characterizing DNA of interest completely by characterizing complementary fragments of all possible lengths.

Southern et al teach cleaving each fragment in a mass spectrometer to release its mass label; and determining each mass label by mass spectroscopy to identify the fragment (page 20, line 7-page 21, line 23) but they do not teach the cleavage is via collision. However, cleaving fragments in a mass spectrophotometer by collision was well known in the art at the time the claimed invention was made as taught by Withers et al. Withers et al further teach a motivation to use collision cleavage i.e. collision cleavage is sufficient to break the ester bond between the mass label and the fragment but does not break bonds within the fragment (Column 19, lines 38-45). Therefore, It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the collision cleavage taught by Withers et al to the mass label cleavage of Southern et al for the expected benefit of mass label-cleavage without damaging the fragment as taught by Withers et al (Column 19, lines 38-45).

Double Patenting

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 1-18, 20-24 and 27-28 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-16 of U.S. Patent No.

6,270,976. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to method for characterizing (analyzing) nucleic acids and differ only in the arrangement of the limitations within the claims and further in that the instant claims include the additional step of separating the nucleic acid by capillary electrophoresis and collision cleavage and the '976 method include the additional steps of ionizing the nucleic acids. However, the instant claim language "comprising" encompasses the additional method step of ionizing recited in the patent claims. Furthermore, more the patent teaches the preferred embodiment includes the step of size separation via capillary electrophoresis (Column 3, lines 30-49) and collision cleavage (Column 4, lines 58-64). Therefore, because the preferred embodiment of the patent method includes the instantly claimed steps of capillary electrophoresis and collision cleavage, the instantly claimed methods are obvious in view of the patent method.

10. Claims 1-18, 20-24 and 27-28 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 33-45 of U.S. Patent No. 6,287,780. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to method for characterizing (analyzing) nucleic acids and differ only in the arrangement of the limitations within the claims and further in that the instant claims include the additional step of separating the nucleic acid by capillary electrophoresis and collision cleavage. However, the patent teaches the preferred embodiment includes the step of size separation via capillary electrophoresis (Column 11, line 60-Column 12, line 8) and collision cleavage (Column 4, lines 24-30). Therefore, because the preferred embodiment of the patent method includes the instantly claimed steps of capillary

electrophoresis and collision cleavage, the instantly claimed methods are obvious in view of the patent method.

11. Claims 1-18, 20-24 and 27-28 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 63-80 of U.S. Patent No. 10/221,666. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to method for characterizing nucleic acids and differ only in the arrangement of the limitations within the claims and further in that the instant claims include the additional step of separating the nucleic acid by capillary electrophoresis and collision cleavage. However, more the '666 application teaches the preferred embodiment includes the step of size separation via capillary electrophoresis (¶ 219) and collision cleavage (¶ 33). Therefore, because the preferred embodiment of the '666 method includes the instantly claimed steps of capillary electrophoresis and collision cleavage, the instantly claimed methods are obvious in view of the patent method.

Conclusion

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (571) 272-0741 until 13 January 2004. The examiner can normally be reached on 6:00 TO 3:30 Monday through Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-0507.

BJ Forman, Ph.D.
Primary Examiner
Art Unit: 1634
January 30, 2004